I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted today via the Office electronic filing system in accordance with §1.6 (a)(4).

Date: November 23, 2009 Signature: _____
Matthew Zischka
(Reg .No. 41,575)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE HONORABLE BOARD OF PATENT APPEALS AND INTERFERENCES

Application No.	:	10/601,378	Confirmation No. 7906
Applicant	:	David Farrow	
Filed	:	June 23, 2003	
Title	:	NANO AND MICRO-TECHNOLOGY VIRUS DETECTION METHOD AND DEVICE	
TC/Art Unit	:	1631	
Examiner	:	Karlheinz R. Skowronek	
Attorney Docket No.	:	93292-1	
Customer No.	:	22463	

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450
U.S.A.

Dear Sir:

APPELLANT'S REPLY BRIEF UNDER 37 C.F.R. 41.41

This is in response to the Examiner's Answer, mailed September 22, 2009.

Status of Claims

Claims 1-5, 7, 8 and 22-29 are pending in this application and stand rejected. Claims 1-5, 7, 8 and 22-29 are being appealed.

The Examiner indicated that the status of the claims provided in the Appeal Brief is not correct. However, the revised Appellant's Brief, filed July 15, 2009, recites the same status of the claims as that indicated by the Examiner.

Grounds of rejection to be reviewed on appeal

A. Rejection of claims 1-5, 7, 8 and 22-29 under 35 U.S.C. 103 as obvious having regard to Tullis et al., *American Clinical Laboratory* (2001) Oct/Nov, 22-23 (hereinafter "Tullis"), in view of US 6,391,657 (hereinafter "Bernhardt"), in view of US 2002/0042125 (hereinafter "Petersen"), in view of newly cited WO 01/85341 (hereinafter "Piesold"); and

B. Rejection of claims 1-5, 7, 8 and 22-29 under 35 U.S.C. 103 as obvious having regard to US 2004/0072278 (hereinafter "Chou"), in view of Bernhardt, in view of newly cited Piesold.

Argument

The Examiner addressed his arguments to all of claims 1-5, 7, 8 and 22-29 and the following marks will therefore also apply to all of claims 1-5, 7, 8 and 22-29. The relevant features are found in each of the independent claims, 1, 22 and 26.

First Ground of Rejection

In rejecting the claims under the first ground of rejection, the Examiner (at page 11 of the Examiner's Answer) relies on Piesold to provide the testing within the second chamber for the presence of residual particles. The Examiner is not correct. Piesold does not detect the presence of residual particles left in a chamber following a filtering step. Piesold describes detection of reaction byproducts. Piesold is directed to a flow-through apparatus for performing miniaturized assay. The portion of Piesold relied on by the Examiner (page 3, lines 24-26), refers to trapping particles within a chamber and then monitoring the particles. There is no mention of residual particles and no mention that the presence of residual particles is indicative of presence of an analyte particle in the original sample. As indicated on page 13, lines 18-32 of Piesold, a bead with an attached pre-hybridized template/primer is trapped in the reaction chamber by the filter. A reaction mixture containing light generating components is added and any light generated in the subsequent reaction is detected with a CCD camera. Thus, testing is not for the presence of residual particles. Rather, light generated by reacting the particles within the chamber is detected. As well, the trapped particles will be in the chamber regardless of the nature of the beads contained in the original sample loaded into the device, and thus the presence of particles trapped in the chamber do not identify the presence of a reagent-analyte complex. Accordingly, Piesold does not disclose, describe or suggest the testing for the presence of residual particles as required by the present claims.

The Examiner also argues that Tullis describes two filtering steps. In particular, the Examiner argues (at page 12 of the Examiner's Answer) that reaction of the viral particle with be beaded agarose with covalently attached antibodies results in formation of analyte-reagent complex that is larger than the selected pore size of the filter. This is an incorrect

interpretation of Tullis. Tullis indicates at page 22, top of second column, that the antibodies are coupled to a "beaded agarose or silica solid support". Thus, the antibodies are immobilized on the solid support of the device within the extra-fiber space. In terms of pore size selection, Tullis only describes the pore size as designed to prevent preformed blood elements from exiting the hollow fibers and flowing into the extra fiber space (page 22, bottom of first column). There is no reason to believe that the antibody/virus complex is larger than the pore size or to believe that if the antibodies were not immobilized within the device, the antibody/viral particle complex could not flow back into the hollow fibers along with the other blood components not originally excluded by the pore size cutoff. Accordingly, Tullis only describes one filtering step, not two, in contrast to the present claims.

The Examiner argues that the wording of claim 1 is broad and encompasses ex situ testing as described in Tullis. First, claim 1 recites "testing said further filtered sample in said second chamber for the presence of residual particles". Thus, claim 1 clearly specifies that testing occurs in the second chamber. Second, Applicant points out that Tullis does not describe detecting residual particles, the presence of which indentifies the presence of a reagent-analyte particle complex. Tullis refers to testing for the virus directly by performing PCR analysis (page 23, first column, third full paragraph).

The Examiner points to excerpts from the references to provide motivation to combine the references. In particular, the Examiner points to a portion of Piesold and relies on this portion as a motivation for miniaturizing experiments and assays. However, the excerpt from Piesold cited by the Examiner indicates that widening the device at the position of the filter allows for more holes in the filter, reducing clogging of the filter, which enhances the feasibility of miniaturizing many experiments and assays currently performed in test tubes and microtiter plates. This physical arrangement of the Piesold device is incompatible with the hollow fiber device of Tullis, and thus would not motivate a skilled person to combine Piesold and Tullis. The Examiner also points to Bernhardt as providing motivation to increase the size of the analyte capture molecule. In fact, Bernhardt indicates that when removing virus particles from a solution by filtration, using the antibodies allows for removal

of smaller viruses and for increased pore size, which increases flow rate. However, in Tullis the pore sizes are designed only to prevent flow of large blood elements from the hollow fibers into the extra fiber space, and thus are already maximally sized to permit flow from the extra fiber space back into the hollow fiber. In Tullis, the virus particle is isolated by capture with an immobilized antibody and it is not the pore size that is involved in isolating the virus. Accordingly, Applicant submits that the motivation relied on by the Examiner would not motivate the skilled person to modify the references to produce the presently claimed invention.

Thus, Applicant submits that the Examiner has failed to demonstrate that the cited combination of references provides all of the claimed elements and has failed to point to a motivation for a skilled person to combine the cited combination of references. Applicant submits that the rejection of claims 1-5, 7, 8 and 22-29 as obvious in light of the combination of Tullis, Bernhardt, Petersen and Piesold should be reversed.

Second Ground of Rejection

In combining Chou, Bernhardt and Piesold, the Examiner relies on Piesold for providing the suggestion of forming a reagent-analyte complex within a chamber and detecting the complex within a reaction chamber. The comments provided above that address the Piesold reference are also relevant to this ground of rejection.

The Examiner refers (at page 14 of the Examiner's Answer) to Examples 15 and 26 in Chou as using the presence of the analyte in a filter chamber as an indicator of the analyte being present in the original sample. However, the present claims recite testing for the presence of residual particle, the presence of which indentifies the presence of reagent-analyte particle, rather than testing for the presence of analyte. Example 15 in Chou describes that suitable characteristics of the trapped particles may be analyzed (see paragraph [0662] in Chou). Chou is describing directly detecting the analyte particle itself and does not describe detection of residual particles as an indication of the presence of a reagent-analyte complex.

The Examiner relies on the same excerpt from Piesold and Bernhardt relied on in the first ground of rejection, to provide motivation to combine these references, along with excerpts from Chou. The excerpts from Chou relate to general advantages of microfluidic methods over large scale methods, such as smaller sample volume, speed, etc., and not to any advantages that are specific to any particular device configuration or separation method. As stated above, the excerpt from Piesold relied on by the Examiner merely indicates that widening the device at the position of the filter can prevent clogging. The excerpt from Bernhardt indicates that increasing the size of a larger particle that is to be retained by a filter can allow for larger pore size and thus can increase flow rate. However, since in Examples 15 and 26 of Chou, and in Piesold, the particle of interest is already larger than the pore size and is already being retained by the filter, the motivation would merely be to increase the size of a particle that is already retained. Thus, the motivation relied on by the Examiner would not provide motivation to modify the cited references to produce the method of the present claims. The Examiner has not pointed to any motivation that would result in the specific sequence and combination of filtration, specific interaction and testing for residual particles in the chamber in which the specification interaction occurs that is claimed in the present claims.

The Examiner states that a skilled person would have a reasonable expectation that the presently claimed method would work, since the method of Bernhardt is demonstrated to be successful. However, this does not address the fact that the cited combination of references does not describe all of the elements of the presently claimed methods and does not motivate combination and modification to arrive at the presently claimed methods. The fact that a very different method is successful at cleaning virus from a sample cannot provide, in the absence of prior knowledge of the presently claimed invention, the expectation that a multi-step process for detection of analyte in a sample that does not arise from the combination of cited references would be successful.

Applicant reiterates the position that the Examiner has failed to demonstrate that the cited combination of references provides all of the claimed elements and has failed to point to a motivation for a skilled person to combine the cited combination of references. Applicant

submits that the rejection of claims 1-5, 7, 8 and 22-29 as obvious in light of the combination of Chou, Bernhardt and Piesold should be reversed.

General

For clarity, in addition to the above submissions, all of the arguments made in the Applicant's Appeal Brief are maintained.

In view of the foregoing, early favourable reconsideration of this application is respectfully requested.

Respectfully submitted,

Matthew Zischka
Registration No. 41,575

SMART & BIGGAR
438 University Avenue
Suite 1500, Box 111
Toronto, Ontario
Canada M5G 2K8
Telephone: (416) 593-5514
Facsimile: (416) 591-1690

November 23, 2009

(93292-1 MZ:SAH:kep)